

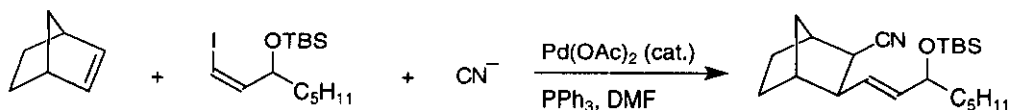
PALLADIUM-MEDIATED FORMATION OF *N*-ACYL-2-HYDROXYINDOLINES: A NEW ENTRY INTO *N*-ACYLINDOLES

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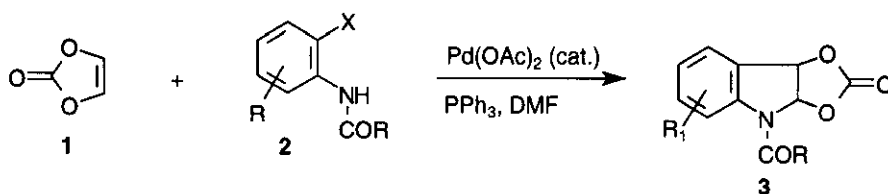
Abstract — *N*-Acyl-2-iodoanilines were reacted with vinylene carbonate in the presence of palladium(II) acetate to give *N*-acyl-2-hydroxyindolines, in good yields, which on acid treatment afforded the corresponding *N*-acylindoles.

Recently, Torii and co-workers¹ have reported an efficient palladium-mediated tandem three-component coupling process to construct the prostaglandin analogues (Scheme 1). Thus, the reaction allowed the coupling of norbornene with a halo olefin and cyanide to give stereoselectively a 2,3-substituted



Scheme 1

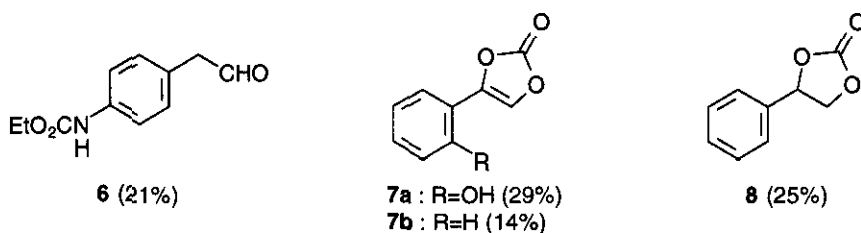
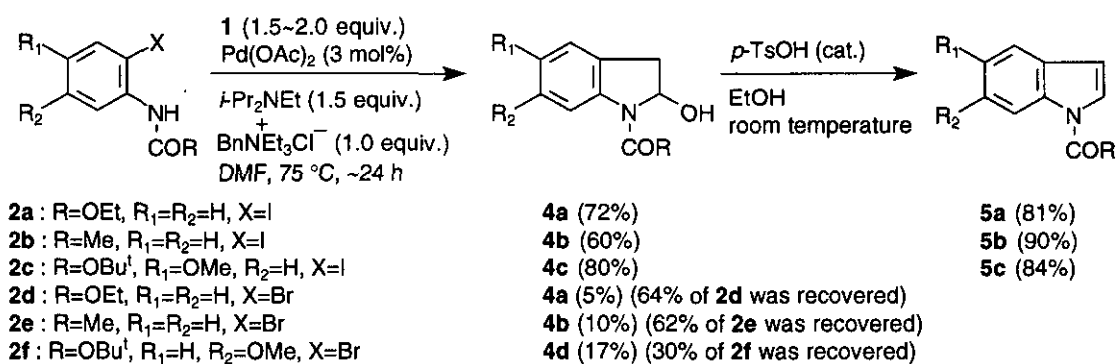
norbornane in a satisfactory yield. Since we were interested in using an aromatic halide carrying a nucleophilic center in the same molecule in this reaction, we examined the reaction between vinylene carbonate (1) and an *o*-iodoaniline derivative (2) under the same palladium-mediated conditions. We expected that the iodoaniline (2) would behave as the two components in the Torii's precedents¹ to add to



Scheme 2

the fixed double bond of vinylene carbonate (**1**) to generate potentially useful 2,3-indolinyll carbonates (**3**) (Scheme 2). We present here the results which led to a new entry into *N*-acylindole derivatives though the reaction was found to proceed in an unexpected way.

Thus, *N*-ethoxycarbonyl-2-iodoaniline (**2a**) was treated with 1.5–2 equiv. of vinylene carbonate (**1**) in DMF containing each a little excess of diisopropylethylamine and benzyltriethylammonium chloride in the presence of 3 mol% of palladium(II) acetate at 75 °C.² The reaction terminated after 2 h and the product obtained in 72% yield was found to be not the initially expected 2,3-indolinyll carbonate (**3**) but the 2-hydroxyindoline (**4a**). The structure of the product (**4a**) was confirmed by transformation into *N*-ethoxycarbonylindole (**5a**) in 81% yield on stirring in ethanol containing a catalytic amount (5 mol%) of *p*-toluenesulfonic acid at room temperature for 13 h. The reaction generally occurred with other *N*-acyl-2-iodoanilines (**2b**, **c**) to give the corresponding 2-hydroxyindolines (**4b**, **c**) in comparable yields under the same conditions from which the corresponding *N*-acylindoles (**5b**, **c**) were obtained in excellent yields. However, the reaction proceeded very slow with 2-bromoaniline derivatives (**2d–f**) which gave the 2-hydroxyindoline (**4a**, **b**, **d**) in poor yields. Interestingly, the reaction proceeded sluggishly when benzyltriethylammonium chloride was absent.

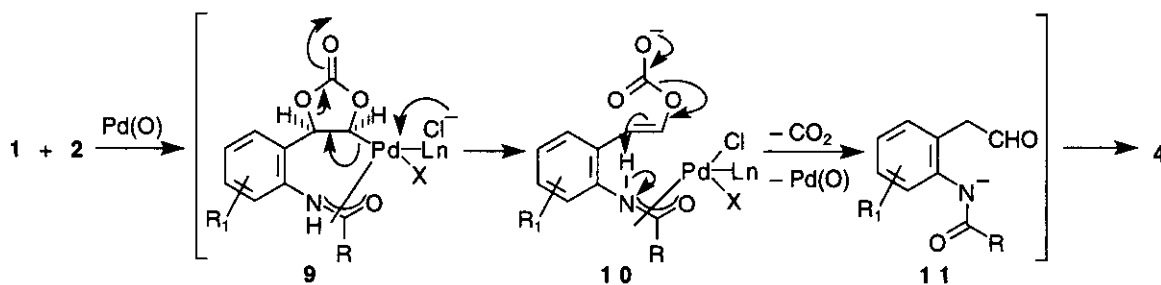


Scheme 3

When *N*-ethoxycarbonyl-4-iodoaniline was treated with vinylene carbonate (**1**) under the same conditions, 4-*N*-ethoxycarbonylaminophenylacetaldehyde (**6**) was obtained in 21% yield indicating that the reaction

necessitated a proximal nitrogen atom to give a better yield. On the same treatment, 2-iodophenol furnished the Heck type product³ (7a) in 29% yield as an only isolable product. Iodobenzene did not yield any coupling product under the same conditions, but it afforded the Heck type product (7b) in 14% yield in the presence of acetic acid and phenylethylene carbonate (8) in 25% yield in the presence of formic acid⁴ (Scheme 3).

Taking into account these findings, a plausible reaction pathway forming the 2-hydroxyindolines (4) is illustrated as shown in Scheme 4. Thus, oxidative addition of the aryl iodide (2) to Pd(0), followed by insertion of the arylpalladium generated to vinylene carbonate (2) produces the complex (9) having internal complexation of which Pd atom is then attacked by chloride ion to initiate E2 type elimination giving rise to the enol carbonate complex (10). Finally, decarboxylation occurs to initiate reductive elimination to produce the penultimate intermediate (11) and Pd(0), the latter of which was recycled.



Scheme 4

ACKNOWLEDGEMENT

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